



Pallister-Hall syndrome

Pallister-Hall syndrome is a disorder that affects the development of many parts of the body. Most people with this condition have extra fingers and/or toes (polydactyly), and the skin between some fingers or toes may be fused (cutaneous syndactyly). An abnormal growth in the brain called a hypothalamic hamartoma is characteristic of this disorder. In many cases, these growths do not cause any health problems; however, some hypothalamic hamartomas lead to seizures or hormone abnormalities that can be life-threatening in infancy. Other features of Pallister-Hall syndrome include a malformation of the airway called a bifid epiglottis, an obstruction of the anal opening (imperforate anus), and kidney abnormalities. Although the signs and symptoms of this disorder vary from mild to severe, only a small percentage of affected people have serious complications.

Frequency

This condition is very rare; its prevalence is unknown.

Genetic Changes

Mutations in the *GLI3* gene cause Pallister-Hall syndrome. This gene provides instructions for making a protein that controls gene expression, which is a process that regulates whether genes are turned on or off in particular cells. By interacting with certain genes at specific times during development, the *GLI3* protein plays a role in the normal shaping (patterning) of many organs and tissues before birth.

Mutations that cause Pallister-Hall syndrome typically lead to the production of an abnormally short version of the *GLI3* protein. Unlike the normal *GLI3* protein, which can turn target genes on or off, the short protein can only turn off (repress) target genes. Researchers are working to determine how this change in the protein's function affects early development. It is uncertain how *GLI3* mutations can cause polydactyly, hypothalamic hamartoma, and the other features of Pallister-Hall syndrome.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits a mutation in the *GLI3* gene from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- Hall-Pallister syndrome
- PHS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Pallister-Hall syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265220/>

Other Diagnosis and Management Resources

- GeneReview: Pallister-Hall Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1465>
- MedlinePlus Encyclopedia: Epiglottis (Image)
<https://medlineplus.gov/ency/imagepages/19595.htm>
- MedlinePlus Encyclopedia: Imperforate Anus
<https://medlineplus.gov/ency/article/001147.htm>
- MedlinePlus Encyclopedia: Polydactyly
<https://medlineplus.gov/ency/article/003176.htm>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Epiglottis (Image)
<https://medlineplus.gov/ency/imagepages/19595.htm>
- Encyclopedia: Imperforate Anus
<https://medlineplus.gov/ency/article/001147.htm>

- Encyclopedia: Polydactyly
<https://medlineplus.gov/ency/article/003176.htm>
- Health Topic: Brain Malformations
<https://medlineplus.gov/brainmalformations.html>
- Health Topic: Hand Injuries and Disorders
<https://medlineplus.gov/handinjuriesanddisorders.html>
- Health Topic: Toe Injuries and Disorders
<https://medlineplus.gov/toeinjuriesanddisorders.html>

Genetic and Rare Diseases Information Center

- Pallister-Hall syndrome
<https://rarediseases.info.nih.gov/diseases/7305/pallister-hall-syndrome>

Educational Resources

- Disease InfoSearch: Pallister-Hall syndrome
<http://www.diseaseinfosearch.org/Pallister-Hall+syndrome/5543>
- MalaCards: pallister-hall syndrome
http://www.malacards.org/card/pallister_hall_syndrome
- Orphanet: Pallister-Hall syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=672

Patient Support and Advocacy Resources

- Hope for Hypothalamic Hamartomas
<http://www.hopeforhh.org/>
- National Organization for Rare Disorders
<https://rarediseases.org/rare-diseases/pallister-hall-syndrome/>
- Resource list from the University of Kansas Medical Center
<http://www.kumc.edu/gec/support/palshall.html>

GeneReviews

- Pallister-Hall Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1465>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Pallister-Hall+syndrome%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28pallister-hall+syndrome%5BTIAB%5D%29+OR+%28hall-pallister+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- PALLISTER-HALL SYNDROME
<http://omim.org/entry/146510>

Sources for This Summary

- Biesecker LG, Abbott M, Allen J, Clericuzio C, Feuillan P, Graham JM Jr, Hall J, Kang S, Olney AH, Lefton D, Neri G, Peters K, Verloes A. Report from the workshop on Pallister-Hall syndrome and related phenotypes. Am J Med Genet. 1996 Oct;2(65):76-81.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/8914745>
- Boudreau EA, Liow K, Frattali CM, Wiggs E, Turner JT, Feuillan P, Sato S, Patsalides A, Patronas N, Biesecker LG, Theodore WH. Hypothalamic hamartomas and seizures: distinct natural history of isolated and Pallister-Hall syndrome cases. Epilepsia. 2005 Jan;46(1):42-7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15660767>
- GeneReview: Pallister-Hall Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1465>
- Johnston JJ, Olivos-Glander I, Killoran C, Elson E, Turner JT, Peters KF, Abbott MH, Aughton DJ, Aylsworth AS, Bamshad MJ, Booth C, Curry CJ, David A, Dinulos MB, Flannery DB, Fox MA, Graham JM, Grange DK, Guttmacher AE, Hannibal MC, Henn W, Hennekam RC, Holmes LB, Hoyme HE, Leppig KA, Lin AE, Macleod P, Manchester DK, Marcelis C, Mazzanti L, McCann E, McDonald MT, Mendelsohn NJ, Moeschler JB, Moghaddam B, Neri G, Newbury-Ecob R, Pagon RA, Phillips JA, Sadler LS, Stoler JM, Tilstra D, Walsh Vockley CM, Zackai EH, Zadeh TM, Brueton L, Black GC, Biesecker LG. Molecular and clinical analyses of Greig cephalopolysyndactyly and Pallister-Hall syndromes: robust phenotype prediction from the type and position of GLI3 mutations. Am J Hum Genet. 2005 Apr;76(4):609-22. Epub 2005 Feb 28.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15739154>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1199298/>
- Johnston JJ, Sapp JC, Turner JT, Amor D, Aftimos S, Aleck KA, Bocian M, Bodurtha JN, Cox GF, Curry CJ, Day R, Donnai D, Field M, Fujiwara I, Gabbett M, Gal M, Graham JM, Hedera P, Hennekam RC, Hersh JH, Hopkin RJ, Kayserili H, Kidd AM, Kimonis V, Lin AE, Lynch SA, Maisenbacher M, Mansour S, McGaughran J, Mehta L, Murphy H, Raygada M, Robin NH, Rope AF, Rosenbaum KN, Schaefer GB, Shealy A, Smith W, Soller M, Sommer A, Stalker HJ, Steiner B, Stephan MJ, Tilstra D, Tomkins S, Trapane P, Tsai AC, Van Allen MI, Vasudevan PC, Zabel B, Zunich J, Black GC, Biesecker LG. Molecular analysis expands the spectrum of phenotypes associated with GLI3 mutations. Hum Mutat. 2010 Oct;31(10):1142-54. doi: 10.1002/humu.21328.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20672375>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2947617/>

- Kang S, Graham JM Jr, Olney AH, Biesecker LG. GLI3 frameshift mutations cause autosomal dominant Pallister-Hall syndrome. *Nat Genet*. 1997 Mar;15(3):266-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9054938>
 - McCann E, Fryer AE, Craigie R, Baillie C, Ba'lath ME, Selby A, Biesecker LG. Genitourinary malformations as a feature of the Pallister-Hall syndrome. *Clin Dysmorphol*. 2006 Apr;15(2):75-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16531732>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/pallister-hall-syndrome>

Reviewed: November 2016

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications

U.S. National Library of Medicine

National Institutes of Health

Department of Health & Human Services